

APPENDIX A

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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NAME Raymond M. Welsh, Ph.D.		POSITION TITLE Professor of Pathology, Molecular Genetics & Microbiology	
eRA COMMONS USER NAME WELSHRM			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of Massachusetts, Amherst	B.S.	1967	Microbiology
University of Massachusetts, Amherst	Ph.D.	1972	Micro/Virology
University of Kansas, Lawrence	Post-Doc	1972-1973	Micro/Biochemistry
Scripps Clinic & Research Foundation, La Jolla, CA	Post-Doc	1973-1975	Virology/Immunology

A. Positions and Honors.**Positions and Employment**

1972-1973 Visiting Assistant Professor of Microbiology, Univ. of Kansas, Lawrence, KS; Dept. of Microbiology

1975-1980 Assistant Member, Scripps Clinic and Research Foundation, La Jolla, CA; Dept. of Immunopathology

1979 Visiting Scientist, Karolinska Institute; Scripps Clinic, 1987.

1980 Adjunct Associate Professor of Pathology, Univ. California at San Diego Medical School, Dept. of Pathology,

1980-1985 Associate Professor of Pathology, Molecular Genetics and Microbiology, Univ. Mass. Medical School, Worcester, MA

1985-Present Professor of Pathology, Molecular Genetics and Microbiology, Univ. Mass. Medical School, Worcester, MA

Honors, Editorial Boards, and Advisory Groups:

Recipient of RCDA AI-00253 (1978-1983); Recipient of NIH Merit Award R37 AI 17672 (2004); Editorial Boards: J. Immunol. (1982-1986; 1997-present) Section Editor (2001); Proc. Soc. Exp. Biol. Med. (1978-1987); J. Virol. (1986-1989; 1991-present; Editor 1998-present); Natural Immunity Cell Growth Regulation (1984-2000); J. Natl. Cancer Inst. (1987-1991); J. Exp. Med. (1995-present); Virology (1996-present); Study Sections: American Cancer Society (National) Immunology and Immunotherapy Section (1988-1991); American Cancer Society (Massachusetts)(1981-1991), Chairman (1985-1991); State of California AIDS Task Force (1985-1996); NIH Virology (1991-1995).

B. Selected peer-reviewed publications (of 221 publications).

Lin MY, and Welsh RM. 1998. Analysis of the stability of T cell receptor (TCR) repertoire usage during lymphocytic choriomeningitis virus (LCMV) infection of mice. J. Exp. Med. 188:1993-2005.

Selin LK, Lin MY, Kraemer KA, Pardoll DM, Schneck JP, Varga SM, Santolucito P, Pinto AK, and Welsh RM. 1999. Attrition of T cell memory: selective loss of LCMV epitope-specific memory CD8 T cells following infections with heterologous viruses. Immunity 11:733-742.

Welsh RM, Markees TG, Woda BA, Daniels KA, Brehm MA, Mordes JP, Greiner DL, and Rossini AA. 2000. Virus-induced abrogation of transplantation tolerance induced by donor-specific transfusion and anti-CD154 antibody. J. Virol. 74:2210-2218.

Selin LK, Santolucito PA, Pinto AK, and Welsh RM. 2001. Innate immunity to viruses: control of vaccinia virus infection by $\gamma\delta$ T cells. J. Immunol. 166:6784-6794.

- Daniels KA, Devora G, Lai WC, O'Donnell CL, Bennett M, and Welsh RM. 2001. Murine cytomegalovirus is regulated by a discrete subset of natural killer cells reactive with monoclonal antibody to Ly49H. *J. Exp. Med.* 194:29-44.
- McNally JM, Zarozinski CC, Lin MY, Brehm MA, Chen HD, and Welsh RM. 2001. Attrition of bystander T cells during virus-induced T cell and interferon responses. *J. Virol.* 75:5965-5976.
- Varga SM, Selin LK, and Welsh RM. 2001. Independent regulation of T cell memory pools: relative stability of CD4 memory under conditions of CD8 memory T cell loss. *J. Immunol.* 166:1554-1561.
- Chen HD, Fraire AE, Joris I, Brehm MA, Welsh RM, and Selin LK. 2001. Memory CD8⁺ T cells in heterologous antiviral immunity and immunopathology in the lung. *Nat. Immunol.* 2:1067-1076.
- Welsh RM and Selin LK. 2002. No one is naive: The significance of heterologous T cell immunity. *Nature Rev. Immunol.* 2:417-426.
- Brehm MA, Pinto AK, Daniels KA, Schneck JP, Welsh RM, and Selin LK. 2002. T cell immunodominance and maintenance of memory regulated by unexpectedly cross-reactive pathogens. *Nature Immunol.* 3:627-634.
- Kim S.-K., Brehm MA, Welsh RM, and Selin LK. 2002. Dynamics of memory T cell proliferation under conditions of heterologous immunity and bystander stimulation. *J. Immunol.* 169: 90-98.
- Brehm MA, Markees TG, Daniels KA, Greiner DL, Rossini AA, and Welsh RM. 2003. Direct visualization of cross-reactive effector and memory allo-specific CD8 T cells generated in response to viral infections. *J. Immunol.* 170:4077-4086.
- Wang XZ, Stepp SE, Brehm MA, Chen HD, Selin LK, and Welsh RM. 2003. Virus-specific CD8 T cells in peripheral tissues are more resistant to apoptosis than those in lymphoid organs. *Immunity* 18:631-642.
- Zipris D, Welsh RM, Mordes JP, Xie JX, Greiner DL, and Rossini AA. 2003. Infections that induce autoimmune diabetes in BBDR rats modulate CD4⁺ CD25⁺ T regulatory cell populations. *J. Immunol.* 170:3592-3602.
- Peacock CD, Kim S -K, and Welsh RM. 2003. Memory T cell attrition: reduced capacity of bona-fide memory CD44^{hi} CD8⁺ T cells to respond to homeostatic and poly I:C-induced proliferation. *J. Immunol.* 171:655-663.
- Kim SK and Welsh RM. 2004. Comprehensive and lasting loss of memory CD8 T cells and functional memory during acute and persistent viral infections. *J. Immunol.* 172:3139-3150.
- Selin LK and Welsh RM. 2004. Plasticity of T cell memory responses to viruses. *Immunity* 20:5-16.
- Welsh RM, Selin LK, and Szomolanyi-Tsuda E. 2004. Immunological memory to viral infections. *Ann. Rev. Immunol.* 22:711-743.
- Kim M, Yang H, Kim S-K, Reche PA, Tirabassi RS, Hussey RE, Chishti Y, Rheinwald JG, Morehead TJ, Damon I, Welsh RM, and Reinherz EL. 2004. Biochemical and functional analysis of smallpox growth factor (SPGF) and anti-SPGF monoclonal antibodies. *J. Biol. Chem.* 279:2538-49.
- Peacock CD and Welsh RM. 2004. Origin and fate of lymphocytic choriomeningitis virus-specific CD8⁺ T cells coexpressing the inhibitory NK cell receptor Ly49G2. *J. Immunol.* 173:478-84.
- Gavanesu I, Pihan G, Halilovic E, Szomolanyi-Tsuda E, Welsh RM, and Doxsey S. 2004. Mycoplasma infection induces a scleroderma-like centrosome autoantibody response in mice. *Clin Exp Immunol.* 2004 137:288-97.
- Wang XZ, Brehm MA, and Welsh RM. 2004. Pre-apoptotic phenotype of viral epitope-specific CD8 T cells precludes memory development and is an intrinsic property of the epitope. *J. Immunol.*, 173:5138-5147.
- Jellison, E. R., S.-K. Kim, and R. M. Welsh. 2005. Cutting edge: MHC class II-restricted killing in vivo during viral infection. *J. Immunol.* 2005 Jan 15;174:614-8.
- Kim, S.-K., X.Z. Wang, M. Cornberg, H.D. Chen, L.K. Selin, and R.M. Welsh. 2005. Private specificities of CD8 T cell responses control patterns of heterologous immunity. *J. Exp. Med.* 2005 Feb 21;201:523-33
- Yang, H., Kim, S.-K., Kim, M., Reche, P. A., Moorehead, T. J., Damon, I. K., Welsh, R. M., and Reinherz, E. L. 2005. Antiviral chemotherapy facilitates control of poxvirus infections through inhibition of cellular signal transduction. *J. Clin. Invest.* 2005 Feb;115:379-87.
- Brehm, M.A., Daniels, K.A., Ortaldo, J.R., Welsh, R.M. 2005. Rapid conversion of effector mechanisms from NK to T cells during virus-induced lysis of allogeneic implants in vivo. *J. Immunol.* 174: (11): 6663-71.

C. Research Support

Ongoing Research Support

ACTIVE:

T32 AI07349-17 Raymond Welsh (PI) 07/01/02-06/30/07

NIH

Training in immunology

Role: PI

This is a training grant that awards pre- and post-doctoral fellowships to trainees in the University of Massachusetts Immunology and Virology Program.

2 R37 AI17672-27 Raymond Welsh (PI) 04/15/04-03/31/09

NIH

Immunity and virus disease

This merit award examines T cell apoptosis and memory T cell loss during viral infection. The specific aims are to (1) determine the mechanism and significance of the early cytokine-induced lymphopenia and apoptosis of memory CD8 T cells during viral infections, (2) determine the mechanisms regulating the tissue-dependent differences in apoptosis of virus-specific CD8 T cells, and (3) determine the mechanism and significance of memory T cell attrition following acute and persistent viral infections

Role: PI

PO1 AI46629-08 Aldo Rossini (PI) 09/01/03- 2/29/08

NIH

Viral infection influence on transplantation tolerance

Role: Raymond Welsh is Co-Investigator

This is a program project grant in which Raymond Welsh is a Project Leader in a section designed to look at the ability of viral infections to induce rejection of skin allografts in mice tolerized by an anti-CD40 ligand protocol and to determine whether the rejection is mediated by T cells cross-reactive between viral and allo-antigens.

PO1 AI49320-06 Katherine Luzuriaga (PI) 06/01/06 -05/31/11

NIH

Ontogeny and maintenance of virus specific T cells

Role: Co-investigator on a project with Liisa Selin as primary investigator

This is a program project to examine human T cell responses to viruses. The purpose of this project is to examine human virus-specific T cells that are cross-reactive between heterologous viruses and to determine if they can be correlated with the pathogenesis of human disease. A focus is on T cell cross-reactivity between influenza virus and Epstein Barr virus.

1 U19 AI-57330-03 Ellis Reinherz, PI 09/01/03 - 03/31/08

NIH

Orthopox immunization in normals and patients with cancer.

This is a program project subcontracted to me from Harvard, where Ellis Reinherz, MD, is PI. The purpose of this grant is to develop better vaccines and treatments for small pox. Most of the animal work for this Program Project will be done at the UMMS Department of Animal Medicine by Raymond Welsh. This includes analyzing the immunology and pathogenesis of vaccinia virus mutants and in testing the efficacy of therapeutic antibodies and drugs against vaccinia virus in mouse models.

Role: Co-Investigator on a Project with Elliot Kieff (Harvard) as primary investigator

RO1 AR35506-20 Raymond Welsh (PI) 01/01/04-12/31/09

NIH

Virus-induced immunopathology

Role: PI

This proposal examines the evolution of the T cell repertoire during viral infections of mice and examines how crossreactive T cells may regulate the control of unrelated viruses.

Completed within the past 3 years

R01 CA34461 Raymond Welsh (PI) 02/01/01-1/31/06

NIH

Regulation of NK cells

Role: PI

This proposal examined the interphase between innate and adaptive immunity to viral infections in mouse models. The specific aims were to (1) examine the role of NKR on $\alpha\beta$ T cell development during viral infection; (2) examine the antiviral activity of $\gamma\delta$ T cells during vaccinia virus infection; (3) evaluate negative signaling NKR in control of infections by T and NK cells; and (4) examine redundancies, synergisms, and antagonisms between NK and T cell responses to viruses.